Remarks/Arguments

The foregoing amendments to the claims are of a formal nature and do not add new matter. Claims 119-131 were pending in this application and are rejected on various grounds. Claims 127-128 and 132-134 have been canceled without prejudice or disclaimer. Claims 119-123 now recite the functional recitation "wherein said polypeptide induces chondrocyte redifferentiation," support for which is also found in the instant specification at least in Example 159, page 530. Claims 139-144 have been added; support for these claims are found in the instant specification, at least in Example 170- the "gene amplification assay". Further, all pending claims have been amended to remove references to "Figures" and the extracellular domain. The rejections to the presently pending claims are respectfully traversed.

Formal Matters

The title of the invention has been amended to describe, more particularly, what the Applicants considers is their invention. Entry of this amendment is respectfully requested.

IDS

Applicants submit an IDS separately enlisting references recited in the Blast report in order to be compliant with 37 C.F.R. § 1.98(a)(1). Consideration of this Information Disclosure Statement is respectfully requested.

Priority

The nucleic acid sequence of SEQ ID NO: 228 and the polypeptide of SEQ ID NO: 229 were first disclosed in U.S. provisional application 60/096,768, filed August 17, 1998, hence Applicants are entitled to an effective filing date of **August 17, 1998,** at least for the sequences of SEQ ID NO: 228 and SEQ ID NO: 229.

Further, Applicants rely on the 'gene amplification' assay (Example 143) for patentable utility of the subject matter relating to claims 119-123. This utility was first disclosed in the US Provisional Application 60/141,037, filed June 23, 1999, priority for which has been claimed in this application. Hence, the present application is at least entitled to an effective filing date of

June 23, 1999 based on results of the 'gene amplification' assay. A copy of the relevant pages from this provisional application are attached for the Examiner's convenience.

Further, Applicants rely on the 'chondrocyte proliferation' assay (Example 153) for patentable utility of the subject matter relating to claims 119-123. This utility was first disclosed in International Application PCT/US00/08439, filed March 30, 2000, priority for which has been claimed in the instant application. Hence, the present application is at least entitled to an effective filing date of **March 30, 2000** based on results of the 'chondrocyte proliferation' assay. A copy of the relevant pages from this provisional application are attached for the Examiner's convenience.

The Examiner has acknowledged utility for the claimed nucleic acids based on the chondrocyte redifferentiation assay. As per the Examiner's request, Applicants have provided a copy of the relevant portion of the PCT application, whose specification is identical to the instant application, that contains the chondrocyte redifferentiation assay for priority determination.

The Examiner further indicates that the gene amplification assay was not found to be enabling as required by the 35 U.S.C.§ 112, first paragraph. The Examiner indicates that the amplification was "mild" and also says that "a slight amplification of a gene does not necessarily mean overexpression in a cancer tissue, but can merely be an indication that the cancer tissue is aneuploid". The Examiner quotes an exemplary reference like Sen and concludes that "the data was not corrected for aneuploidy". Applicants submit that, as noted by the Examiner and the Sen article, aneuploid tissues are cancerous or pre-cancerous. The present invention is directed to nucleic acids useful in the detection of cancer, irrespective of the mechanism by which gene amplification occurs. Even if aneuploid tissues were to predict a propensity for cancer, the instant nucleic acids are still useful as diagnostic tools. Applicants have included a declaration by Avi Ashkenazi, Ph.D., a co-inventor of this application, who says that:

> "An increase in gene copy number can result not only from intrachromosomal changes but also from chromosomal aneuploidy. It is important to understand that detection of gene amplification can be used for cancer diagnosis even if the determination includes measurement of chromosomal aneuploidy. Indeed, as long as a significant difference relative to normal tissue is detected, it is irrelevant if the signal originates from an increase in the number of gene copies per chromosome and/or an abnormal number of chromosomes."

Thus, even if the tissue were aneuploid, nucleic acids encoding PRO1111 would still be useful in detecting tissues with a propensity towards cancer.

Therefore, Applicants have demonstrated utility for the PRO1111 encoding nucleic acids based on the "chondrocyte proliferation assay" as well as the "gene amplification assay" and thus, Applicants request that the Examiner reconsider the priority date for the present application based on the present arguments.

Claim Rejections – 35 USC § 112, second paragraph

Claims 119-138 were rejected under 35 U.S.C. §112, second paragraph for being indefinite.

The Examiner says that the recitation "extracellular domain" and "lacking its associated signal sequence" were indefinite.

Without acquiescing to the propriety of this rejection and without limitations to pursuing this subject matter in future applications, merely to expedite prosecution in this case, Applicants have canceled references to "the extracellular domain" in the pending claims.

Claims are vague and indefinite since the claims recite "hybridizes" without recitation of any conditions.

Applicants have canceled claims without prejudice or disclaimer. New claims recite the exact hybridization conditions; support for these claims can be found in the instant specification at least at pages 312-313. Accordingly, this rejection should be withdrawn.

Claim Rejections – 35 USC § 112, first paragraph

Claims 119-124, 126-128 and 132-138 are also rejected under 35 U.S.C. §112, first paragraph because, according to Examiner, "the specification, while being enabling for SEQ ID NO: 228 or fragments usable as hybridization probes, or nucleic acids which encode the protein of SEQ ID NO: 229 for making antibodies or that have chondrocyte differentiation activity, does not reasonably provide enablement for nucleic acids having at least 80%, 85%, 90%, 95% or 99% sequence identity to SEQ ID NO:228. Applicants respectfully traverse this rejection.

Claims 119-123 now recite the functional recitation "wherein said polypeptide induces chondrocyte redifferentiation" and is therefore enabled, as agreed by the Examiner. This rejection is inappropriately applied to claim 124 since it is already enabled as acknowledged by the Examiner. Claims 127-128 and 132-134 have been canceled and hence, this rejection is moot for these claims. Claims 135-138 depend either directly or indirectly upon claims 119 and 124, both of which are enabled. New claims 139-145 are also enabled since the probes hybridize to "an isolated nucleic acid molecule consisting of a fragment of the nucleic acid sequence of SEQ ID NO: 228 or a complement thereof," which is enabled.

Hence, reconsideration of this rejection is requested in view of recent claim amendments and should be withdrawn.

Claim Rejections - 35 USC § 112, first paragraph- written description

Claims 119-124, 126-128 and 132-138 are rejected under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing.

As discussed above, specific utilities have been asserted for the presently pending claims 119-123 that now recite the functional recitations "wherein said polypeptide induces chondrocyte redifferentiation" and for claims 139-145 useful in the diagnosis of lung or colon cancer. Since the claims are drawn to a genus of polypeptides defined both by sequence and functional identity, it would have been obvious to one skilled in the art at the effective priority date, in view of Applicant's possession of the nucleic acid of SEQ ID NO:228, that the Applicant possessed these obvious variations and adaptations of SEQ ID NO:228 at the time of filing.

Hence, Applicants request that the present rejection be reconsidered and withdrawn.

Deposit requirement

The Examiner pointed out that the deposit of biological material made under the Budapest Treaty for enablement of the current invention needs the current address of the ATCC and a declaration or statement stating that all restrictions imposed by the depositor on the public be irrevocably removed. Applicants submit that requisite assurances have been added into the

specification to remove, irrevocably, all restrictions imposed by the depositor on the availability of deposited material to the public upon the granting of the pertinent U.S. patent. Accordingly, this rejection should be withdrawn.

Claim Rejections - 35 USC § 102

Claims 119-123 and 132-138 are rejected under 35 U.S.C. §102(a) or 102(b) as being anticipated by loci AI769814, AI435407, AI470931, and under 35 U.S.C. 102(b) as being anticipated by locus T15752.

Applicants submit that loci AI769814, AI435407, AI470931 and T15752 are ESTs that have 21.88, 20.46, 17.98 and 21.5 overall percent identity to the nucleic acid sequence of SEQ ID NO: 228. The current claims are directed to sequences with 80-100% sequence identity to the nucleic acid sequence of SEQ ID NO: 228. Therefore, none of these EST sequences anticipate the current claims and hence, this rejection under 35 U.S.C. §102(a) or 102(b) should be withdrawn.

Claims 119-124, 127-128 and 132-138 are rejected under 35 U.S.C. §102(a) or 102(b) as being anticipated by Jacobs et al. (WO 99/50405, pub date 10/7/99).

As discussed above, Applicants are at least entitled to an effective filing date of **June 23, 1999** for the nucleic acid sequence of SEQ ID NO: 228 based on a substantial, credible and specific utility, the 'gene amplification' assay. Therefore, Jacobs is not prior art and this rejection should be withdrawn.

Claims 119-124, 127-128 and 130-131 are rejected under 35 U.S.C. §102(e) as being anticipated by Shimkets, USPN 6,689,866 or US patent Pub US2003/0054514 or US patent Pub US2003/0003532 (dated 3/8/00).

As discussed above, Applicants are at least entitled to an effective filing date of **June 23, 1999** for the nucleic acid sequence of SEQ ID NO: 228 based on a substantial, credible and specific utility, the 'gene amplification' assay. Therefore, Shimkets is not prior art and this rejection should be withdrawn.

The present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-2730P1C56). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: December 6, 2004

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